Amendments to the Claims

This listing will replace all prior versions of the claims, and the prior listing of claims in the application:

1. (Original) A method of inhibiting angiogenesis or tumorigenesis in a biological sample, comprising

    a. providing a biological sample; and

    b. combining the sample with an angiogenesis-inhibiting or tumorigenesis-inhibiting amount of a composition comprising an inhibitor of apelin activity.

2. (Original) The method of Claim 1, wherein the composition decreases vascular permeability in the biological sample.

3. (Original) The method of Claim 1, wherein the composition interferes with the interaction of an apelin polypeptide or apelin peptide with a receptor polypeptide.

4. (Original) The method of Claim 1, wherein the composition interferes with the interaction of an apelin polypeptide or apelin peptide with APJ.

5. (Original) The method of Claim 1, wherein the composition further comprises an anti-cancer agent and wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic agent, a radiotherapeutic agent, an anti-angiogenesis agent, and an apoptosis-inducing agent.

6. (Original) The method of Claim 5, wherein the composition comprises an anti-angiogenesis agent that inhibits an angiogenic factor selected from the group consisting of VEGFs, FGFs, PDGFB, EGF, LPA, HGF, PD-ECF, IL-8, angiogenin, TNF-alpha, TGF-beta, TGF-alpha, proliferin, and PLGF.

7. (Original) The method of Claim 1, wherein the composition comprises an anti-apelin antibody or fragment thereof.

8. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds a polypeptide that is selected from the group consisting of:

a. a polypeptide as defined in SEQ ID NO:1;

b. a polypeptide as defined in SEQ ID NO:2;

c. a polypeptide as defined in SEQ ID NO:3;

d. a polypeptide as defined in SEQ ID NO:4;

e. a polypeptide as defined in SEQ ID NO:5; and

f. a polypeptide having at least 80% sequence identity with the polypeptide of a) through e) above.

9. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide of SEQ ID NO:1.

10. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide of SEQ ID NO:2.

11. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide of SEQ ID NO:3.

12. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide of SEQ ID NO:4.

13. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds the polypeptide as defined in SEQ ID NO:5.

14. (Original) The method of Claim 7, wherein the antibody or fragment thereof binds a polypeptide that has at least 90% sequence identity with the polypeptide or peptide of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:5 and that interacts with APJ.

15. (Original) The method of Claim 1, wherein the inhibitor of apelin activity is an anti-APJ antibody or fragment thereof.

16. (Original) The method of Claim 15, wherein the antibody or fragment thereof binds a polypeptide as defined in SEQ ID NO:17.

17. (Original) The method of Claim 15, wherein the antibody or fragment thereof binds a polypeptide having at least 80% sequence identity with the polypeptide as defined in SEQ ID NO:17.

18. (Original) The method of Claim 1, wherein the inhibitor of apelin activity is selected from the group consisting of an apelin antisense nucleic acid, receptor decoy, ribozyme, sense polynucleotide, double stranded RNA, RNAi, aptamer, and small molecule antagonist.

19. (Original) The method of Claim 1, wherein the inhibitor of apelin activity is selected from the group consisting of an APJ antisense nucleic acid, receptor decoy, ribozyme, sense polynucleotide, double stranded RNA, RNAi, aptamer, and small molecule antagonist.

20. (Original) The method of Claim 1, wherein the inhibitor of apelin activity is an inhibitor of a serine protease that cleaves a polypeptide specifically after an arginine residue.

21. (Original) The method of Claim 1, wherein the composition comprises a pharmaceutically acceptable carrier.

22. (Original) The method of Claim 1, wherein the biological sample is from a mammal.

23. (Original) The method of Claim 1, wherein the biological sample is a human biological sample.

24. (Original) The method of Claim 23, wherein the biological sample is in a patient.

25. (Original) The method of Claim 24, wherein the composition is introduced by a route selected from the group consisting of subcutaneous injection, intravenous injection, intraocular injection, intradermal injection, intramuscular injection, intraperitoneal injection, intratracheal administration, epidural administration, inhalation, intranasal administration, oral administration,

sublingual administration, buccal administration, rectal administration, vaginal administration, and topical administration.

26. (Original) The method of Claim 24, wherein the patient has a disease or condition involving angiogenesis or tumorigenesis.

27. (Canceled)

28. (Original) The method of Claim 24, further comprising

c. administering to the patient a therapeutically effective amount of an anti-cancer agent, wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic agent, a radiotherapeutic agent, an anti-angiogenic agent, an apoptosis-inducing agent.

29. (Original) The method of Claim 28, wherein the anti-cancer agent is an anti-angiogenic agent.

30. (Original) The method of Claim 28, wherein the anti-angiogenic agent is an inhibitor of an angiogenic factor selected from the group consisting of VEGFs, FGFs, PDGFB, EGF, LPA, HGF, PD-ECF, IL-8, angiogenin, TNF-alpha, TGF-beta, TGF-alpha, proliferin, and PLGF.

31. (Original) A method of decreasing vascular permeability in a biological sample, comprising

a. providing a biological sample from a patient; and

b. combining the sample with a vascular permeability-decreasing amount of a composition comprising an inhibitor of apelin activity.

32. (Canceled)

33. (Original) A method of promoting angiogenesis in a biological sample, comprising

a. providing a biological sample; and

b. combining the sample with a biologically effective amount of an angiogenesis promoting composition comprising apelin activity.

34. (Original) The method of Claim 33, wherein the composition further comprises an angiogenic factor selected from the group consisting of VEGFs, FGFs, PDGFB, EGF, LPA, HGF, PD-ECF, IL-8, angiogenin, TNF-alpha, TGF-beta, TGF-alpha, proliferin, and PLGF.

35. (Original) The method of Claim 33, wherein the angiogenesis promoting composition comprises a serine protease that cleaves a polypeptide specifically after an arginine residue.

36. (Original) The method of Claim 33, wherein the composition comprises a polypeptide selected from the group consisting of:

a. a polypeptide as defined in SEQ ID NO:1;

b. a polypeptide as defined in SEQ ID NO:2;

c. a polypeptide as defined in SEQ ID NO:3;

d. a polypeptide as defined in SEQ ID NO:4;

e. a polypeptide as defined in SEQ ID NO:5; and

f. a polypeptide having at least 80% sequence identity with the polypeptide of a) through e) above.

37. (Original) The method of Claim 33, wherein the composition comprises the polypeptide as defined in SEQ ID NO:1.

38. (Original) The method of Claim 33, wherein the composition comprises the polypeptide as defined in SEQ ID NO:2.

39. (Original) The method of Claim 33, wherein the composition comprises the polypeptide as defined in SEQ ID NO:3.

40. (Original) The method of Claim 33, wherein the composition comprises the polypeptide as defined in SEQ ID NO:4.

41. (Original) The method of Claim 33, wherein the composition comprises the polypeptide as defined in SEQ ID NO:5.

42. (Original) The method of Claim 33, wherein the composition comprises a small molecule agonist.

43. (Original) The method of Claim 33, wherein the apelin composition comprises a polypeptide that has at least 90% sequence identity with the polypeptide or peptide of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:5; and that interacts with APJ.

44. (Original) The method of Claim 33, wherein the biological sample is from a mammal.

45. (Original) The method of Claim 33, wherein the biological sample is a human biological sample.

46. (Original) The method of Claim 45, wherein the biological sample is in a patient.

47. (Original) The method of Claim 46, wherein the composition is introduced by a route selected from the group consisting of subcutaneous injection, intravenous injection, intraocular injection, intradermal injection, intramuscular injection, intraperitoneal injection, intratracheal administration, epidural administration, inhalation, intranasal administration, oral administration, sublingual administration, buccal administration, rectal administration, vaginal administration, and topical administration.

48. (Original) The method of Claim 33, wherein the composition comprises a pharmaceutically acceptable carrier.

49. (Original) The method of Claim 46, wherein the patient has a disease or condition that is indicated by decreased vascularization.

50. (Original) The method of Claim 49, wherein the disease or condition is selected from the group consisting of diabetes, arthritis, ischemia, anemia, a wound, gangrene, or necrosis.

51. (Original) A method for identifying a modulator of angiogenesis, comprising

a. providing an angiogenesis promoting composition comprising apelin;

b. combining a putative modulator of angiogenesis with the composition;

c. introducing the composition or the combination of the putative modulator and the composition to an angiogenesis predictive model; and

d. comparing the amount of vascular branching in the model in the presence and absence of the putative modulator.

52. (Original) The method of Claim 51, wherein the composition comprises a polypeptide selected from the group consisting of:

a. a polypeptide as defined in SEQ ID NO:1;

b. a polypeptide as defined in SEQ ID NO:2;

c. a polypeptide as defined in SEQ ID NO:3;

d. a polypeptide as defined in SEQ ID NO:4;

e. a polypeptide as defined in SEQ ID NO:5; and

f. a polypeptide having at least 80% sequence identity with the polypeptide of a) through e) above.

53. (Original) The method of Claim 51, wherein the composition comprises the polypeptide as defined in SEQ ID NO:1.

54. (Original) The method of Claim 51, wherein the composition comprises the polypeptide as defined in SEQ ID NO:2.

55. (Original) The method of Claim 51, wherein the composition comprises the polypeptide as defined in SEQ ID NO:3.

56. (Original) The method of Claim 51, wherein the composition comprises the polypeptide as defined in SEQ ID NO:4.

57. (Original) The method of Claim 51, wherein the composition comprises the polypeptide as defined in SEQ ID NO:5.

58. (Original) The method of Claim 51, wherein the composition comprises a polypeptide that has at least 90% sequence identity with the polypeptide or peptide of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:5, and that interacts with APJ.

59. (Original) The method of Claim 51, wherein the angiogenesis predictive model is a chicken chorioallantoic membrane (CAM) assay.